UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

CASWELL FILE

DATE: July 27, 1979

SUBJECT: Section 18 Emergency Specific Exemption, use of Pirimiphos-methyl on Farmers Stock Peanuts in Georgia.

Caswell #334B

FROM: John Doherty (7/27/79) 7/27/79
Toxicology Branch/HED (TS-769)

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

TO: Don Rodier
Special Registration Section, RD (TS-767)

THRU: M. Adrian Gross William M. Butler for M. Adrian Gross
Chief, Toxicology Branch/HED (TS-769)

Note: This Section 18 request was previously denied by Toxicology Branch because use of the active ingredient was not toxicologically supported (see J. Doherty memo; April 13, 1979; to Hoyt Jamerson). This request is now being reconsidered following submission of additional toxicological data.

1) The state of Georgia is requesting to use 2,960 gallons (20,720 lb. a.i.) of pirimiphos-methyl on approximately 60% of this state's peanut crop (on approximately 518,000 tons of peanuts). The pesticide will be applied within the various peanut store houses at the time the peanuts will be put into storage. Only one application will be made at an amount equivalent to 20 ppm on these peanuts.

2) The formulation to be used will be ACTELLIC 7E (not currently registered with EPA). The human hazard signal word is WARNING and available toxicity data support this signal word.

The proposed label must be changed to correct the "Note to Physician:" to clearly state that 2-PAM or P-25 (pralidoxime) is effective only when given with atropine. There is no evidence that pralidoxime given alone is effective (see reviewed data in PP 2G2154).

3) According to the request prepared by the State of Georgia Department of Agriculture, the residues resulting from the use of ACTELLIC in accordance with this proposed program would be 2 ppm or less in the kernel and 10 ppm or less in the hull.

4) There are no existing tolerances for pirimiphos-methyl.

5) Using a NOEL (for ChE inhibition) of 10 ppm obtained from the rat 2 year study and a 10 fold safety factor, the % ADI occupied will be 2.92%. Without this Section 18 exemption, the % ADI occupied will be 0% since no other uses of pirimiphos-methyl have as yet been approved.

In determining the % ADI used up by this Section 18 exemption, residues in cattle, etc. were included since peanuts are fed to animals as feed.

6) Synopsis of Toxicity (Technical Material)

Test	Result	CORE Classification
Intraperitoneal LD_{50}, rats	800 mg/kg	Supplementary
Oral LD_{50}, rats, females	2050 mg/kg	Supplementary
Oral LD_{50}, mice, males	1180 mg/kg	Supplementary
Oral LD_{50}, guinea pigs, females	1000-2000 mg/kg	Supplementary
Oral LD_{50}, rabbits, males	1000-2000 mg/kg	Supplementary
Oral LD_{50}, cats	575-1150 mg/kg	Supplementary
Oral LD_{50}, hens	31-62 mg/kg	Supplementary
Oral LD_{50}, dogs	>1500mg/kg	Supplementary
Dermal LD_{50}, rats, females	>2000 mg/kg	Supplementary
Dermal Irritation, rats	not irritating	Minimum
Eye Irritation, rabbits	not irritating	Supplementary
Subacute oral, rats 10 doses orally (gavage) (200 and 400 mg/kg)	i) 200 mg/kg/day weight loss, Hb decease, other blood and spleen injuries	Supplementary
	ii) 400 mg/kg/day 65% mortality	Supplementary
Subacute dermal, rabbits	1000 mg/kg, loss in weight, 1 death	Supplementary
Subacute Inhalation, rats	3.5 ppm, no toxic signs	Supplementary
Sensitization, guinea pigs	Not a sensitizer	Supplementary
Subacute oral, dogs (90 day)	NOEL ≤ 2 mg/kg/day for RBC ChE inhibition. Systemic NOEL is >25 mg/kg/day (liver damage)	Minimum
Oncogenesis, mouse (18 month)	No compound related	Minumum
(0, 5, 250, 500 ppm)	tumors. At 5 ppm, RBC ChE inhibition occasionally significant.	
Dominant lethal, mouse (150 mg/kg)	negative	Minimum
Mutagenicity (Ames test)	Mutagenic (?)	Invalid
Teratology, rabbits (0, 1, 16 mg/kg)	Not teratogenic	Supplementary
Reproduction, rats, study #1 (0, 20, 200 ppm)	Decreased fertility at 20 ppm (?)	Minimum

Reproduction, rats, study #2 (0, 5, 10, 100 ppm)	No effects	Minimum
Human exposure	No effects, 0.25 mg/kg/day, 28 days, oral administration. Some cholinesterase effects, 0.25 mg/kg/day, 56 days, oral administration.	Supplementary
Neurotoxicity, chickens	Some undefined lesions at 50-60 mg/kg	Supplementary
Subacute oral, rats (90 day) (0, 8, 80, 360 ppm)	ChE inhibition at 80 and 360 ppm. NOEL = 8 ppm	Minimum
2 year chronic feeding/ Oncogenesis, rats (0, 10, 50, 300 ppm)	NOEL = 10 ppm for ChE inhibition. No systemic effects at 50 and 300 ppm.	Minimum
2 year chronic feeding, dogs (0, 0.5, 2.0, 10.0 mg/kg/day)	NOEL $\leq$ 0.5 mg/kg/day (brain ChE is 20% below control)	Guidelines

(The above synopsis of toxicity was taken from a review of pesticide petition 9G2154, by J. Doherty, in preparation).

7) John Shaughnessy, EPA, has informed Toxicology Branch, by telephone conversation on 7/24/79, that one inert ingredient in the proposed formulation (ACTELLIC 7E) is not cleared for this post-harvest use. In addition, there is some question as to whether or not a second inert is cleared or not for this use. John Shaughnessy will contact the manufacturer about these inerts.

8) It is noted that Residue Chemistry Branch (see review by J. Worthington, dated 6/27/79) has recommended against granting this proposed Section 18 Exemption. The reasons for this recommendation include:

   A.) "The degradation of pirimiphos-methyl in peanut meats is not adequately understood at this time. Further characterization of the make-up of the terminal residue in this commodity is needed."

   B.) "Additional characterization of the components of the terminal residue in milk, eggs and poultry is needed."

   C.) "--- the studies submitted to date indicate that the parent compound comprises, at most, a small portion of the total residue."

9) For the reasons given in 7.) and 8.) above, Toxicology Branch can not recommend in favor of granting this Section 18 Exemption until these issues are satisfactorily resolved. It is to be noted, furthermore, that pending the results from 8.) above regarding the identification and quantification of terminal residues in peanut meats, milk, eggs, and poultry, Toxicology Branch may request additional toxicity studies on these terminal residues.

7/26/79

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